COMPOSITIONS CONTAINING TOPICAL ACTIVE AGENTS AND PENTYLENE GLYCOL

BACKGROUND OF THE INVENTION

[0001] Hydrocortisone is used in many topical preparations as a treatment for temporary relief of itching associated with minor skin irritation, inflammation and rashes due to eczema, insect bites, poison ivy, poison oak, poison sumac, soaps, detergents, cosmetics, seborrheic dermatitis, psoriasis and itching in the genital and anal areas of the body. Hydrocortisone has limited solubility in water. Thus, it is necessary to add co-solvents, surfactants, and/or complexing agents to obtain an aqueous solution of hydrocortisone in sufficient concentration to be therapeutically efficacious.

[0002] U. S. Patent 2,880,130 discloses the use of polyoxyethylene sorbitan monooleate (Tween 80®) in amounts of from 2-25 percent of the vehicle to obtain clear aqueous solutions containing up to 0.2% of hydrocortisone. U. S. Patent 4,289,764 describes formulations containing 0.025 to 0.4% hydrocortisone in an aqueous solution of 15-50% propylene glycol that is acidified to pH 2.7-3.3 with a non-toxic organic acid such as citric acid. U. S. Patent 4,305,936 provides for a 0.005-2.5% hydrocortisone clear liquid formulation containing 1-4% by weight of a glyceryl ester of fatty acids having 6-22 carbon atoms, 1-3% by weight of the hydrocortisone of a betaine surfactant, and 10-50% of an alkanol co-solvent, preferably ethanol. U. S. Patent 4,778,060 describes a 0.5% hydrocortisone aqueous solution for use as a douche and for impregnating towelettes for wipes. The solution also contains caprylic/capric triglycerides (5-20%), sorbitan stearate (2-4%), Polysorbate 60® (1-3%), preservatives and citric acid.

[0003] U.S. Patent 4,383,992 discloses an aqueous solution of an inclusion complex of unbranched beta-cyclodextrin and hydrocortisone and reveals that the inclusion complex must dissociate before the hydrocortisone is physiologically active. U. S. patent 5,229,370 discloses an aqueous solution on an inclusion complex composed of a branched beta-

cyclodextrin and hydrocortisone. U.S. Patent 4,853,379 teaches hydrocortisone compositions containing a mixture of solvents which are an aliphatic alcohol, propylene glycol and dimethyl coco-benzylammonium chloride. U.S. Patent 4,971,789 teaches various ionic polyethers as solubilizers for pharmaceuticals such as hydrocortisone. U.S. Patent 5,190,936 teaches compositions containing hydrocortisone and a lipid phase of nonionic amphiphilic lipid vesicles. GB 2,131,693 teaches hydrocortisone compositions containing a solvent mixture of (i) a caprolactam and (ii) 2-isostearyl-1-hyroxylethyl-1-benzylimidazolinium chloride or an alkylphenol polyglycerol. WO 96/20712 teaches aqueous solutions of hydrocortisone free of lower alcohols that contain sodium dioctyl sulfosuccinate in mixtures of glycerin, propylene glycol and polyethylene glycol.

SUMMARY OF THE INVENTION

[0004] A first aspect of the present invention is directed to a cosmetic or dermatological composition for topical use, comprising a steroidal hormone or anti-inflammatory agent, and a solvent for the hormone or anti-inflammatory agent comprising pentylene glycol.

[0005] A second aspect of the present invention is directed to a method of formulating a steroidal hormone or anti-inflammatory agent for use in a cosmetic or dermatological composition, comprising mixing the steroidal hormone or anti-inflammatory agent and pentylene glycol.

[0006] A third aspect of the present invention is directed to a method of treating skin or scalp, comprising applying to skin or scalp a composition comprising a steroidal hormone or anti-inflammatory agent, and pentylene glycol.

[0007] In preferred embodiments, the steroidal hormone or anti-inflammatory agent is hydrocortisone or a derivative (e.g., an ester) thereof. The compositions of the present invention may be formulated in a variety of ways, e.g., as a gel, emulsion, ointment, shampoo or lotion. They may be applied to skin or scalp for cosmetic or dermatological

purposes e.g., for conditions amenable to treatment with the steroidal hormone or anti-inflammatory agents.

[0008] Applicants have discovered that hydrocortisone is more soluble in pentylene glycol than other polyols and its homologs such as glycerol, propylene glycol, butylene glycol and hexylene glycol. Accordingly, compositions of the present invention may contain less total solvent compared to current products. Compositions of the present invention thus offer more aesthetic appeal. Since steroidal hormones and anti-inflammatory agents must be in solution to permeate skin, the compositions may also offer greater efficacy from the standpoint of delivery.

BRIEF DESCRIPTION OF THE DRAWING

[0009] Figure 1 is a graph comparing cumulative release of hydrocortisone from various commercial products and an embodiment of the present invention, as a function of time.

DETAILED DESCRIPTION

[0010] Any steroid hormone or steroidal anti-inflammatory agent (collectively referred to herein as "active agents") soluble in pentylene glycol (and more soluble in pentylene glycol than in water) and which can be administered transdermally can be used in the present invention. Steroid hormones have post-menopausal, anabolic, contraceptive and anti-inflammatory uses. Representative examples include testosterone and dehydroepiandrosterone (DHEA). Representative examples of steroidal anti-inflammatory agents include fluoracetonide, fludrocortisone, difluorsone diacetate, flurandrenolone acetonide, betamethasone and its other esters, chloroprednisone, desonide, dichlorisone, methylmeprednisolone, cortisone acetate and hydrocortisone cyclopentylpropionate.

[0011] Preferred active agents for use in the present invention are corticosteroids. These are hormonal derivatives that may be prepared synthetically or extracted from the cortex of the adrenal capsules, and which contain a

cyclopentanophenanthrene ring-system. They are particularly useful in the treatment of certain skin diseases, such as contact eczema or atopic dermatitis. Corticosteroids include betamethasone, betamethasone dipronionate, betamethasone phosphate, betamethasone valerate, cortisone, dexamethasone, fludrocortisone, fluocinonide, fluocinonide desonide, fluocinolone, fluocinolone acetonide, fluocortolone, hydrocortisone and its derivatives (e.g., esters thereof such as hydrocortisone 17-valerate, hydrocortisone 17-butyrate and hydrocortisone 21-acetate), methylprednisolone, prednisolone, prednisolone 21-phosphate, prednisone, triamcinolone, triamcinolone acetate and triamcinolone acetonide. More preferred active agents are hydrocortisone and derivatives (e.g., esters e.g., mono- and di-esters, such as hydrocortisone 21-acetate; hydrocortisone 21-benzadac; hydrocortisone 21-cyclopentylpropionate; hydrocortisone 21-hemisuccinate; hydrocortisone 21-acetate 17-propionate; hydrocortisone 17-butyrate; hydrocortisone 17-valerate; and hydrocortisone 17-butyrate 21-propionate.)

[0012] The active agent is present in the compositions in therapeutically effective amounts. In general, the active agent will be present in the composition in an amount of about 0.01 to about 20% by weight. Plainly, however, these amounts will vary depending on the specific active agent. For example, the amount of hydrocortisone (or derivative thereof) in the compositions according to the present invention is generally not greater than about 12% (e.g., about 0.1 to about 12% by weight). Preferably, the hydrocortisone is present in the compositions of the present invention in an amount between 0.01 and 5 % by weight, and more particularly between 0.5 and 4 %, based on the total weight of the composition. These amounts are effective to treat conditions for which hydrocortisone and its salts and esters are indicated, e.g., eczema, atopic dermatitis, psoriatic or eczematous erythrodermy, pruriginous lesions, chronic erythematous lupus, patch psoriasis and parapsoriasis, hyperthrophic cicatrix, and

radiotherapic or solar erythema. Frequency and amount of use of the compositions of the present invention will depend upon numerous factors, including the condition being treated and its severity. For example, application of compositions containing hydrocortisone e.g., to treat one of the conditions disclosed above typically requires an application of the composition of the present invention to the affected area of the skin, on the average, twice each day, optionally with a massaging action in order to facilitate the penetration thereof into the skin.

[0013] Pentylene glycol is typically present in an amount of about 5% to about 70% by weight of the composition. The amount of pentylene glycol used in the composition varies depending on the amount of the active agent and whether it is the only solvent used. For example, Applicants have found that the solubility of hydrocortisone in pentylene glycol is about 6%, which as shown in the Examples below, is higher than the solubility of hydrocortisone in other glycols. Thus, in embodiments where pentylene glycol is the only solvent, and hydrocortisone (or a derivative thereof) is present, the pentylene glycol is present in an amount of about 16-17 times the amount of the hydrocortisone. Other solvents (or "co-solvents"), particularly non-volatile solvents, may be present in the composition. These solvents include esters, polyols, such as glycerin, propylene glycol, butylene glycol and hexylene glycol, polyethylene glycols, polypropylene glycols, and mixtures thereof. Additional solvents may be present in an amount of about 5% to about 50% by weight of the composition. In preferred embodiments, pentylene glycol is present in amounts of about 5% to about 25%, and other solvents present in amounts of about 10% to about 70% of the total weight of the composition. Due to the greater solubility of the active agents in pentylene glycol, the amounts of the other solvents are significantly lower e.g., about 20 to about 95% less, than if pentylene glycol were not present. Relatively high amounts of glycols are undesirable

from several standpoints, especially in terms of aesthetic appeal and tackiness. In contrast, compositions of the present invention are more aesthetically acceptable and have less tackiness.

[0014] The compositions according to the present invention can be provided in various forms, principally in the form of emulsions (e.g., creams), gels, lotions and shampoos. They may also be in anhydrous form e.g., in the form of an ointment, gel or pomade. Emulsions and gels are preferred. Compositions of the present invention other than those in anhydrous form have an aqueous phase and an oil or fatty phase. When the composition according to the invention is an emulsion, the proportion of the fatty phase generally ranges from about 0.5% to about 80% by weight and preferably from about 5% to about 50% by weight, based on the total weight of the composition. Oils, waxes, emulsifiers and co-emulsifiers that are typically present in the composition may be selected from those conventionally used in cosmetics and dermatology.

[0015] The fatty phase or oily phase usually contains at least one oil. Examples include hydrocarbon-based oils of animal origin, such as perhydrosqualene; hydrocarbon-based oils of plant origin, such as liquid triglycerides of fatty acids containing from 4 to 10 carbon atoms, for instance heptanoic or octanoic acid triglycerides or alternatively, for example, sunflower oil, corn oil, soybean oil, marrow oil, grapeseed oil, sesame oil, hazelnut oil, apricot oil, macadamia oil, arara oil, sunflower oil, castor oil, avocado oil, caprylic/capric acid triglycerides, jojoba oil or karite butter oil; synthetic esters and synthetic ethers, especially of fatty acids, for instance oils of formulae R^6COOR^7 and R^6OR^7, in which R^6 represents a fatty acid residue containing from 8 to 29 carbon atoms, and R^7 represents a branched or unbranched hydrocarbon-based chain containing from 3 to 30 carbon atoms, such as, for example, purcellin oil, isononyl isononanoate, isopropyl myristate, 2-ethylhexyl palmitate, 2-octyl-dodecyl stearate, 2-octyldodecyl erucate or isostearyl isostearate;

hydroxylated esters such as isostearyl lactate, octyl hydroxystearate, octyldodecyl hydroxystearate, diisostearyl malate, triisocetyl citrate and fatty alkyl heptanoates, octanoates and decanoates; polyol esters such as propylene glycol dioctanoate, neopentyl glycol diheptanoate and diethylene glycol diisononanoate; and pentaerythritol esters such as pentaerythrityl tetraisostearate; linear or branched hydrocarbons of mineral or synthetic origin, such as volatile or non-volatile liquid paraffins, and derivatives thereof, petroleum jelly, polydecenes, and hydrogenated polyisobutene such as parleam oil; fatty alcohols containing from 8 to 26 carbon atoms, such as cetyl alcohol, stearyl alcohol and a mixture thereof (cetylstearyl alcohol), octyldodecanol, 2-butyloctanol, 2-hexyldecanol, 2-undecylpentadecanol, oleyl alcohol or linoleyl alcohol; alkoxylated and ethoxylated fatty alcohols such as oleth-12; partially hydrocarbon-based and/or silicone-based fluoro oils such as perfluoromethylcyclopentane, perfluoro-1,3-dimethylcyclohexane, perfluoro-1,2-dimethylcyclo-butane; perfluoroalkanes such as dodecafluoropentane and tetradecafluorohexane, bromoperfluorooctyl; nonafluoromethoxybutane and nonafluoro-ethoxyisobutane; perfluoromorpholine derivatives, such as 4-trifluoromethylperfluoromorpholine; silicone oils such as volatile or non-volatile polymethylsiloxanes (PDMSs) containing a linear or cyclic silicone chain, and that are liquid or pasty at room temperature, e.g., cyclopolydimethyl-siloxanes (cyclomethicones) such as cyclohexa-siloxane; polydimethylsiloxanes comprising alkyl, alkoxy or phenyl groups, that are pendent or at the end of a silicone chain, these groups containing from 2 to 24 carbon atoms; phenylsilicones, such as phenyltrimethicones, phenyldimethicones, phenyltrimethylsiloxydiphenylsiloxanes, diphenyldimethicones, diphenylmethyldiphenyltrisiloxanes, 2-phenylethyl-trimethylsiloxysilicates and polymethylphenyl-siloxanes; and mixtures thereof.

[0016] Other fatty substances that may be present in the oily phase are, for example, fatty acids containing from 8 to 30 carbon atoms, such as stearic acid, lauric acid, palmitic acid and oleic acid; waxes of animal origin, such as lanolin, beeswax, spermaceti or lanolin derivatives, such as lanolin alcohols, hydrogenated, hydroxylated or acetylated lanolin, lanolin fatty acids and acetylated lanolin alcohol; waxes of vegetable origin, such as carnauba, candelilla, kapok, ouricury, rice, hydrogenated jojoba, esparto or japan wax or cork fibre or sugar cane waxes or cocoa butter; mineral waxes, for example paraffin, montan, lignite or petrolatum waxes or microcrystalline waxes, ceresin or ozokerite; or synthetic waxes, such as polyethylene waxes, waxes obtained by the Fischer-Tropsch synthesis and linear esters resulting from the reaction of a saturated C_{10} to C_{40} carboxylic acid and of a saturated C_{10} to C_{40} alcohol, such as myristyl myristate. Use may also be made of cetyl alcohol, stearyl alcohol, calcium lanolates or stearates, castor oil, palm oil, coconut oil, sunflower oil or hydrogenated coconut oil; gums such as silicone gums (dimethiconol); silicone resins such as trifluoromethyl-C1-4-alkyldimethicone and trifluoro-propyldimethicone; and silicone elastomers. These fatty substances may be chosen in a varied manner to prepare a composition having the desired properties, e.g., consistency or texture.

[0017] Emulsions may contain at least one emulsifier e.g., amphoteric, anionic, cationic and nonionic emulsifiers, used alone or as a mixture. Choice of emulsifier depends upon the nature of the emulsion e.g., water-in-oil (W/O) or oil-in-water (O/W) emulsions. Examples of emulsifiers that may be used in O/W emulsions include nonionic emulsifiers such as saccharide esters and ethers such as sucrose stearate, sucrose cocoate (and mixtures of sucrose stearate and cocoate); polyol esters, in particular glycerol or sorbitol esters, such as glyceryl stearate, polyglyceryl-2 stearate and sorbitan stearate; glycerol ethers; oxyethylenated and/or

oxypropylenated ethers such as the oxyethylenated, oxypropylenated ether of lauryl alcohol containing 25 oxyethylene groups and 25 oxypropylene groups (CTFA name "PPG-25 laureth-25") and the oxyethylenated ether of the mixture of C_{12}-C_{15} fatty alcohols containing 7 oxyethylene groups (CTFA name "C_{12}-C_{15} Pareth-7"); ethylene glycol polymers such as PEG-100, and mixtures thereof.

[0018] Examples of emulsifiers for use in W/O emulsions include fatty esters of a polyol, in particular of glycerol or of sorbitol, and in particular polyol isostearates, oleates and ricinoleates; saccharide esters and ethers such as methyl glucose dioleate; fatty esters such as magnesium lanolate; dimethicone copolyols and alkyldimethicone copolyols.

[0019] Examples of surfactants (emulsifying and coemulsifying) include the esters of fatty acids and polyethylene glycol (PEG), esters of fatty acids and glycerol (glyceryl stearate) or esters of fatty acids and sugar (sorbitan stearate), as well as the polyoxyethylenated or polyoxypropylenated derivatives thereof, cyclomethicones and dimethicone copolyols, and also anionic surfactants (e.g., potassium or sodium alkyl phosphates).

[0020] Gels are obtained using gelling agents such as cellulose derivatives (e.g., ethyl cellulose), carboxyvinyl polymers (Carbopols), natural or synthetic gums, modified clays (bentones), metal salts of fatty acids (aluminum stearate), ethylene/acrylate copolymers, silicas and polyethylenes. The gelling agent is typically used in an amount of about 0.5 and about 15 %, based on the total weight of the composition.

[0021] Lotions generally contain the active agent e.g., hydrocortisone or salt or ester thereof, solubilized in pentylene glycol, optionally with one or more additional solvents. The ointments are anhydrous compositions based, for example, on petrolatum, paraffin oil or waxes.

[0022] Other cosmetically or dermatologically acceptable agents that may be used in the compositions of the invention include coloring agents (pigments, dyes, colorants e.g., iron oxides, titanium oxides and zinc oxides), preservatives, perfumes and fragrances, hydrating active agents, ultraviolet ray-absorbing agents (sunscreen or sunblock agents), pulverulent agents, antiperspirants and/or odor absorbers, moisturizers, for example protein hydrolysates and polyols such as glycerol, glycols, for instance polyethylene glycols, and sugar derivatives; natural extracts; procyannidol oligomers; vitamins, for instance vitamin A (retinol), vitamin C (ascorbic acid), vitamin E (tocopherol), vitamin B5 (panthenol) and vitamin B3 (niacinamide); vitamin K; urea; caffeine; depigmenting agents such as kojic acid and caffeic acid; salicylic acid; alpha-hydroxy acids such as lactic acid and glycolic acid; retinoids such as carotenoids; fillers, keratolytic agents, anti-oxidants, melatonin; extracts of algae, fungi, plants, yeasts or bacteria; hydrolysed, partially hydrolysed or unhydrolysed proteins, and enzymes; antibacterial or bactericidal agents e.g., 2,4,4'-trichloro-2'-hydroxydiphenyl ether (triclosan) and 3,4,4'-trichlorocarbanilide (or triclocarban), azelaic acid and benzoylperoxide; matt-effect agents, for instance fibres; tensioning agents; optical brighteners; and mixtures thereof, as well as additional active ingredients aside from the active agents of the present invention. Amounts of such agents typically range from about 0.0001% to about 20% by weight of the composition. For example, U.S. Patent 5,643,898 teaches a combination for inducing and stimulating hair growth, or decreasing hair loss, containing hydrocortisone and a pyrimidine derivative, e.g., Minoxidil. Thus, persons skilled in the art will be able to select additional active ingredients and inert ingredients suitable for administration to skin or scalp as desired. See, e.g., U.S. Patent 5,275,755 (directed to shampoo compositions).

[0023] The following examples are intended to further illustrate certain embodiments of the invention and are not intended to limit the invention in any way. Unless otherwise indicated, all percentages are weight-by-weight.

EXAMPLES

Example 1: Solubility of Pentylene Glycol in Various Solvents

[0024] Fifty (50) grams of each of the following solvents were added to a separate beaker, and stirred with a magnetic stirrer at 50 °C. Hydrocortisone (USP from Pharmacia) was added in increments of 0.2 grams to each beaker until maximum solubility was reached. Maximum solubility was determined visually. The results are shown in Table 1. Hydrocortisone was about 3 times more soluble in pentylene glycol than isopropyl lauroyl sarcosinate, about 2 times more soluble in pentylene glycol than hexylene glycol, about 1.5 times more soluble in pentylene glycol than in propylene glycol and about 1.25 times as soluble in pentylene glycol than butylene glycol.

Table 1

Glycerin:	0.4%
Isopropyl lauroyl sarcosinate:	2.0%
Propylene glycol:	4.0%
Butylene glycol:	4.8%
Pentylene glycol:	6.0%
Hexylene glycol:	3.2%

Example 2: Illustration of Solubilization Capabilities of various Solvents for Hydrocortisone

[0025] Water was added to three different solutions containing 1% hydrocortisone. Each contained a different solvent system, i.e., (1) 30 grams of pentylene glycol, (2) 15 grams pentylene glycol and 15 grams butylene glycol, and (3) 10 grams of each of pentylene glycol, butylene glycol and propylene glycol. Water was added until a precipitate was formed. The amount of water was determined for each solution.

The results are shown in Table 2. They show that a reduction in amount of pentylene glycol had a negative effect on solubility of hydrocortisone - when the amount of pentylene glycol was reduced by two-thirds, the effectiveness of the solvent system was reduced in half.

Table 2

Amount of wated added (gms)	Solvent system
120	30 g pentylene glycol
98	15 g pentylene glycol and 15 g butylene glycol
65	10 g pentylene glycol, 10 g butylene glycol and 10 g propylene glycol

Example 3: Emulsion

Table 3

Phase		INCI Name (Trade Name)	
A		Water	51.800
		Propylene glycol	7.000
		Pentylene glycol	10.000
		Butylene glycol	10.000
		Preservatives	0.300
		Nylon 12	2.000
		Hydrocortisone, USP (Micronized)	1.000
B		Dicaprylyl ether (Cetiol OE)	3.000
		C12-15 Alkyl benzoate	3.000
		Octyl palmitate	3.000
		Isononyl isononaoate	1.000
		Cetyl dimethicone (Abil wax 9801)	1.000
		Cetearyl alcohol and Dicetyl phosphate and Ceteth-10 phosphate (Crodafos CES)	3.600
		Glyceryl monostearate self-emulsifier	1.500
		Preservatives	0.700
C		Polyacrylamide (and) C13-14	1.100

		isoparaffin (and) laureth-7 (Sepigel 305)	
		Total	100.00

[0026] To prepare the composition described in table 3, the batch amount of water was added to the main beaker. The remaining ingredients of phase A were mixed separately and then added to the main beaker. The ingredients of phase B were added to a separate container and mixed at 50 °C until clear. The mixture was allowed to cool to room temperature, and then was added to the main beaker while mixing. The mixing was continued until homogeneous. The ingredients of phase C were mixed in a separate container, followed by the addition of the mixture of phases A and B thereto, while mixing. The batch was homogenized for 5 minutes.

Example 4: Water in Oil Cream

Table 4
Water in oil cream

Phase	INCI Name (Trade Name)	%	500 G
A	Water	40.20	201.00
	Sodium chloride	0.50	2.50
B	Propylene glycol	5.00	25.00
	Pentylene glycol	17.00	85.00
	Butylene glycol	17.00	85.00
	Hydrocortisone	1.00	5.00
C	Cetyl PEG/PPG-10/1 dimethicone (ABIL EM 90)	2.30	11.50
	Octyl palmitate	6.50	32.50
	Cyclopentasiloxane (GE SF 1214)	3.50	17.50
	Cyclopentasiloxane (Dow Corning DC 245)	3.50	17.50
	C12-15 Alkyl benzoate	3.50	17.50
	Total	100.00	500.00

[0027] The batch amount of water was added to the main beaker, followed by addition of sodium chloride while mixing until the sodium chloride was dissolved. The ingredients of phase B were added to a separate container and mixed at 50 °C until clear. The mixture was allowed to cool to room temperature, and then was added to the main beaker while mixing. The mixing was continued until homogeneous. The ingredients of phase C were mixed in a separate container, followed by the addition of the mixture of phases A and B thereto, while mixing. The batch was homogenized for 5 minutes.

Example 5: Cream

Table 5

Cream

Phase	INCI Name (Trade Name)	%	500 G
A	Water	27.60	138.00
	Acrylates/C10-30 alkyl acrylate crosspolymer (Pemulen, Noveon)	0.30	1.50
B	Propylene glycol	5.00	25.00
	Pentylene glycol	20.00	100.00
	Butylene glycol	20.00	100.00
	Hydrocortisone	1.00	5.00
C	Dicaprylyl ether (Cetiol OE)	3.00	15.00
	C12-15 Alkyl benzoate	3.00	15.00
	Octyl palmitate	1.00	5.00
	Isononyl isononaoate	3.00	15.00
	Arachidyl alcohol and behenyl alcohol and arachidyl glucoside (Montanov 202)	2.50	12.50
	Behenyl alcohol	0.50	2.50
D	Triethanolamine	0.10	0.50
	Water	5.00	25.00
E	Glyceryl polyacrylate (Hispagel 200)	8.00	40.00
	Total	100.00	500.00

[0028] The batch amount of water was weighed and added to the main beaker. Pemulen™ was added to the water and homogenized until it was dispersed. The ingredients of phase B were weighed and combined in a separate container and mixed at 50°C until clear, and then added to the main beaker while mixing. Mixing was continued until homogeneous. The ingredients of each of phases C, D and E were weighed and combined in three separate beakers. Phase C ingredients were heated to 80°C and then added to the main beaker (phases A and B) that was also heated to 80°C. The resultant mixture of phases A, B and C was homogenized for 3 minutes, followed by addition of phase D and homogenization for an additional 2 minutes. The resultant batch was cooled to 55°C, followed by addition of phase E, and homogenizing for an additional 3 minutes.

Example 6: Gel

Table 6

Hydrocortisone gel

Phase	INCI Name (Trade Name)	%	500 G
A	Water	40.60	203.00
	Carbomer (carbopol 980)	0.30	1.50
B	Propylene glycol	5.00	25.00
	Pentylene glycol	20.00	100.00
	Butylene glycol	20.00	100.00
	Hydrocortisone	1.00	5.00
C	Triethanolamine	0.10	0.50
	Water	5.00	25.00
D	Glyceryl polyacrylate (Hispagel 200)	8.00	40.00
	Total	100.00	500.00

[0029] The batch amount of water was weighed and added to the main beaker. The ingredients of phase B were weighed and combined in a separate container and mixed at 50°C until clear. Phase B ingredients were cooled to room temperature and added to the main beaker. Carbopol™ was sprinkled in the beaker while mixing. Mixing was continued until all dispersed. All ingredients of phases C and D were weighed and combined each in separate beakers. Phase C was added to the batch while mixing. Mixing was continued until it was clear. Phase D was added to the batch while mixing, which was continued until all clear.

Example 7: Comparison of Release of Hydrocortisone from Embodiment of present invention and various Commercial Products

[0030] The materials used included sodium hydroxide and potassium phosphate monobasic (Malinckrodt Baker, Inc., Paris, KT); hydrocortisone USP (Pharmacia & Upjohn, Kalamazoo, MI);

acetonitrile HPLC grade (Burdick & Jackson, Muskegon, MI); cellulose nitrate membrane filters 0.45 µm x 25mm (Whatman, Maidstone, England); PVDF syringe filters 0.45 µm (Whatman, Clifton, NJ).

[0031] The gel described in Example 6 (the gel of the present invention) was tested against competitive products. Competitor products tested included Cortaid 1% Hydrocortisone Anti-Itch Cream (Pharmacia, Peapack, NJ); Rite Aid Hydrocortisone Cream 1% Plus 12 Moisturizers (Rite Aid, Harrisburg, PA); Cortizone 10 1% Hydrocortisone Anti-Itch Ointment and Cortizone 10 1% Hydrocortisone Anti-Itch Cream (Pfizer, Morris Plains, NJ).

[0032] Dissolution testing was performed using a Van Kel VK 7000 dissolution instrument, a Van Kel VK 750D water bath/circulator and a Van Kel VK 8000 autosampler (Varian, Cary, NC). Formulations were run in triplicates using one-liter vessels with a 7.0 phosphate buffer saline solution as the receptor phase. Paddles mixed at 100 RPM and 0.45 um pore size cellulose nitrate membrane filters were used. The filters were soaked in phosphate buffer saline solution for 10 minutes before dissolution testing. A constant temperature of 32°C was maintained. Samples were taken at 0.5, 1, 2, 3, 4, and 6 hours for fast release products and 1, 2, 4, 6, 12, and 24 hours for slow release products. Sample volumes of 10 ml were taken directly into disposable test tubes and concentrations were calculated with a dilution factor to account for drug and volume taken from the vessels during previous sampling.

[0033] Analysis was conducted using two assay methods. The first method, UV-VIS, entailed use of an Agilent 8453 (Agilent Technologies, Wilmington, DE) UV-Vis spectrophotometer. Absorbance of hydrocortisone was read at 248 nm. HPLC analysis of samples of current marketed products was done using High Performance Liquid Chromatography (HPLC). A Perkin Elmer Series 200 HPLC apparatus (Perkin Elmer, Norwalk, CT)

was used with the detector set at 248 nm. Samples were filtered prior to analysis with 0.45 μm PVDF syringe filters. The mobile phase at time of injection was 30:70 acetonitrile to water. A gradient, increasing the acetonitrile to water ratio to 70:30, was then used to cleanse the column between samples and prepare for the next injection. The injection volume was 10 μL. A Phenomenex Prodigy ODS2 C18 4.6 mm x 25 cm particle size 5 μm column (Phenomenex, Torrance, CA) was used at 30° C. The flow rate was 1 mL/min. The retention time of Hydrocortisone was 10.7 minutes.

[0034] The results are shown in Fig. 1. The release of hydrocortisone from the gel of the present invention was about 100 times greater than the release of hydrocortisone from the Commercial products, none of which contain pentylene glycol. The results show that compositions of the present invention provide greater availability of the active agent to penetrate the affected area on the skin or scalp, and thus provide greater bioavailability of the active agent.

[0035] All publications cited in the specification (e.g., the list of citations below) are indicative of the level of skill of those skilled in the art to which this invention pertains. All these publications are herein incorporated by reference to the same extent as if each individual publication were specifically and individually indicated to be incorporated by reference.

[0036] Although the invention herein has been described with reference to particular embodiments, it is to be understood that these embodiments are merely illustrative of the principles and applications of the present invention. It is therefore to be understood that numerous modifications may be made to the illustrative embodiments and that other arrangements may be devised without departing from the spirit and scope of the present invention as defined by the appended claims.